Alliance of defense: Microscopic enemies in the crosshairs

Bacteria join forces against a common enemy

Two bacterial species cooperate chemically with each other to fight off amoebae that generally consume them. A team of researchers from Jena has now discovered this on coorperation-based defense mechanism of bacteria. In this context, natural substances play an important role. Originally responsible for the communication and interaction of microorganisms, they can provide impulses for the development of new drugs such as antibiotics.

Microorganisms naturally live in communities. They interact with each other and with their environment. Their coexistence is regulated by natural substances, small molecules that cause complex subsequent reactions through their activity. These can be very different: Some species are well-disposed towards each other, whereas some fight each other to death. Representatives of the two bacterial genera *Pseudomonas* and *Paenibacillus* have found a way to jointly defend themselves against their predators, the amoebae. "The two bacterial species and the amoebae share their natural habitats. They live in forest soils, for example, and the bacteria serve as food source for the amoebae," says Pierre Stallforth from the Leibniz Institute for Natural Product Research and Infection Biology - Hans Knöll Institute (Leibniz-HKI) in Jena.

As Stallforth and his team now have discovered, these bacteria are not defenseless against the amoeba's attacks. "When *Pseudomonas* and *Paenibacillus* join forces, they can successfully defend themselves and even defeat their predator," says Stallforth. In the process, *Pseudomonas* forms the lipopeptide syringafactin, which in turn is cleaved by peptidases from *Paenibacillus*. The resulting compounds sometimes have a lethal effect on the amoebae. "We were able to show that an organic compound of one bacterium stimulates the other to produce enzymes. These enzymes break down the organic compound into smaller elements. They are active agents against the threat, able to kill the amoeba. By jointly producing a chemical weapon, the bacteria escape their fate of being eaten. Cooperation can thus be helpful. We think we have discovered just one of many examples of this cooperative strategy," Stallforth explains. The authors of the study report on the natural substances involved in this process in the scientific journal *Proceedings of the National Academy of Sciences of the U.S.A.*

The researchers found out about this defensive alliance by cultivating the involved microorganisms together instead of keeping them isolated from each other, as it usually is the case. "The lack of new active ingredients for drugs requires entering new grounds in natural product research. We try to create conditions in our laboratories that are as close as possible to nature, because we now know that microorganisms behave differently in communities than in pure strains," says Stallforth, who is also involved in the Jena Cluster of Excellence "Balance of the Microverse". In this interdisciplinary research network, the focus is on microbiome research. The cluster scientists are

investigating the interaction of microorganisms in different habitats to conduct overarching principles. These provide approaches to solve urgent societal challenges such as antibiotic resistance, pesticide use in agriculture and climatic changes.

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